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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/155,252	09/21/98	EVANS R	SALK1470-2

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EXAMINER	
BUNNER, B	

ART UNIT	PAPER NUMBER
1647	17

DATE MAILED: 08/15/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/155,252	EVANS ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *16-26* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☒ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *Substitute PTO-948* .

DETAILED ACTION

The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647, Examiner Bridget E. Bunner.

Status of Application, Amendments and/or Claims

The amendment of 29 November 1999 (Paper No. 7) has not been entered because the page and line numbers do not recite any SEQ ID NOs. The amendments of 27 December 2000 (Paper No. 10), and 02 March 2001 (Paper No. 12) have been entered in full. Claims 1-15 are cancelled and claims 24-26 are added.

Election/Restrictions

Applicant's election with traverse of Group II, claims 16-21, drawn to a method of testing compounds in Paper No. 12 (02 March 2001) is acknowledged. The traversal is on the ground(s) that Groups I and II are related since both groups describe methods for modulating the effects of PPAR-γ. Applicant also asserts that the compounds identified by the method of Group II are suitable for the method of Group I and thus, a prior art search of one group would involve a search of the other group. This is not found persuasive because inventions I and II are different methods which require different ingredients, process steps and endpoints. Groups I and II require different method steps, wherein each is not required one for the other. For example, Group I requires search and consideration of testing a compound for its ability to regulate transcription-activating effects of a peroxisome proliferator activated receptor-gamma, which is not required for the other invention. Group II requires search and consideration of efficacy of treatment of obesity and diabetes and administration of a peroxisome proliferator activated receptor-gamma antagonist to a subject, which is not required for the other invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 22-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12 (02 March 2001).

Claims 16-21 are under consideration in the instant application.

Sequence Compliance

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 15, 07 June 2001) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 14, 03 May 2001) are *withdrawn in part* (see paragraph below). The CRF that was submitted for the sequences in the instant application were corrected by the PTO's STIC Systems Branch. Specifically, non-ASCII "garbage" was deleted at the end of the files. Also, STIC Systems Branch changed the margins in cases where the sequence text was "wrapped" down to the next line.

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. **Specifically, the nucleic acid sequences recited in claims 18-19 are not accompanied by the required reference to the relevant sequence identifiers.** Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

The disclosure is objected to because of the following informalities:

4. An updated status of the parent nonprovisional applications should be included in the first sentence of the specification.

5. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "Method of Testing Compounds for Regulation of Transcription of Peroxisome Proliferator Activated Receptor-Gamma".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 16-21 are directed to a method of testing a compound for its ability to regulate transcription-activating effects of a peroxisome proliferator activated receptor-gamma (PPAR-γ) comprising assaying changes in the level of reporter protein as a result of contacting cells containing the receptor and reporter vector with a compound. Further, the claims recite that the reporter vector comprises a promoter, hormone response element, and a DNA segment encoding a reporter protein. The compound is a putative antagonist for the peroxisome proliferator activated receptor-gamma and the cell contacting is carried out in the presence of increasing concentrations of the compound and a fixed concentration of at least one agonist. The claims also recite that the cell contacting is carried out in the presence of at least one PPAR-γ-selective modulator.

The specification teaches that "CV-1 cells are co-transfected with CMX-GAL-PPARγ and pTK-MH100x4-LUC" and "fresh medium containing one concentration of a serial dilution of agonist is added to each well" after an initial 2-3 hour incubation (pg 23, lines 29-30; pg 24, lines 1-11). Luciferase reporter gene assays and β-galactosidase transfection controls are

performed with the data expressed as relative light units per O.D. of β-galactosidase per minute. Furthermore, the specification discloses that "effector plasmid, reporter plasmid, and β-galactosidase control plasmid are co-transfected into CV-1 cells at a ratio of about 1:3:5, using a liposome-mediated method" (pg 24, lines 27-30). After a 2-3 hour incubation, an appropriate prostaglandin is added to the media. Cell aliquots are assayed for luciferase and β-galactosidase activity (pg 25, lines 1-10). However, the specification does not teach transfecting a cell with a reporter vector that comprises a promoter, a hormone response element, and a DNA segment. The specification does not define the components of the pTK-MH100x4-LUC reporter construct (ie, MH100 oligonucleotides) and therefore, it is not clear what hormone response elements, if any, are incorporated into that reporter system. Furthermore, if hormone response elements are incorporated into the pTK-MH100x4-LUC vector, what is the minimal sequence of the response element and how many are present? The specification also does not teach methods or examples to demonstrate that the receptor and the reporter vector are present inside the cell or on the cell surface. Additionally, the specification does not teach contacting the cell that contains the receptor of interest and the reporter vector with a fixed concentration of agonist concomitantly with increasing concentrations of any compound. The specification also does not disclose contacting the cell that contains PPAR-γ and the reporter vector with the combination of any compound and at least one PPAR-γ modulator. Finally, the specification does not teach the values or alterations in the level of the reporter protein that would indicate a compound is capable of regulating transcription activation of PPAR-γ in a cell.

Due to the large quantity of experimentation necessary to determine the sequence of the optimal response element and to regulate transcription activation of PPAR-γ by assaying the

levels of a reporter protein wherein the reporter vector comprises a promoter, a hormone response element, and a DNA segment encoding the reporter, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the incubation of a PPAR-γ/reporter vector cell with any compound and any agonist and incubation of the cell with any compound and any PPAR-γ selective modulator, the complex nature of the invention, and the breadth of the claims which fail to recite any hormone response element limitations and agonist/antagonist/modulator/compound limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Regarding claims 16-21, the phrase "thereof" in claim 16 renders the claims indefinite because it is unclear whether "thereof" refers to the activation of the hormone response element only, activation of the promoter only or activation of both the hormone response element and the promoter.

10. Claims 16-21 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating how the level of a reporter protein has

to change in order to determine that the test compound regulates transcription-activating effects of a PPAR-γ. Does the reporter protein increase? Decrease? Remain the same?

11. The term "modulator" in claim 21 is a relative term which renders the claim indefinite. The term "modulator" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For example, is a "modulator" a compound? A protein? The definition of the word "modulate" at page 11, lines 15-23 of the specification of the instant specification is not clear.

Conclusion

No claims are allowable.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Forman et al. Annals NY Acad Sci 761: 29-37, 1995

Zhang et al. J Biol Chem 271(50): 31771-31774, 1996.

Kliewer et al. Cell 83(5): 813-819, 1995.

Zhu et al. Proc Nat Acad Sci USA 92(17): 7921-7925, 1995.

Tontonoz et al. Nuc Acid Res 22(25): 5628-5634, 1994.

Kliewer et al. Proc Nat Acad Sci USA 91(15): 7355-7359, 1994.

Tontonoz et al. Curr Opin Genet Develop 5(5): 571-576, 1995.

Greene et al. US patent 6,200,802

Evans et al. US patent 5,702,914

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
August 8, 2001

ELIZABETH KEMMERER
PRIMARY EXAMINER